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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,725	09/18/2003	Manabu Nakatani	01-1395	4358

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EXAMINER	
HELM, CARALYNNE E	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,725	NAKATANI ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 6-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 6-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Note to Applicant: References to paragraphs in non-patent literature refers to full paragraphs (e.g. 'page 1 column 1 paragraph 1' refers to the first full paragraph on page 1 in column 1 of the reference)

Response to Arguments

Applicants' arguments, filed February 7, 2008, have been fully considered but they are not deemed to be fully persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The examiner made note of Friedl et al. not teaching a particular variety of the Pluronic® to be used as a solubilizer in the taught invention (see paragraph 63 lines 1 and 11). However, Friedl et al. clearly contemplate its use at 1%-10 wt% within their composition that also included a basic agent, water-soluble diluent, and telmisartan (see paragraphs 49 and 55). The quantity of solubilizer taught overlaps the range taught by the instant claims and explicitly teaches the lower end of the claimed range. Furthermore, Friedl et al. teach that several methodologies could be used to make the solid telmisartan preparation including the coating of carrier particles in a fluidized bed (see paragraph 38 lines 1-4). One of ordinary skill in the art at the time the invention was made would have readily recognized that fluidized bed granulation would meet this recitation (granulating solution is sprayed (coated) onto suspended (fluidized) particles which then dry rapidly in the suspending air – see Gennaro page 1625 column 2 paragraph 1 lines 1-4). Thus the composition taught by Friedl et al. is suitable for fluidized bed granulation. An alternate reference has been used in the rejections that follow to provide the teachings originally gleaned from Gendron et al.

Applicant has presented results that are described as unexpected. These results are neither persuasive nor sufficient to overcome the prior art for several reason. The results detail a dissolution assay of a composition with Pluronic® F68 or without Pluronic® F68 where its use resulted in faster solubilization. The reported use of this compound in a pharmaceutical is as a solubilizing agent in both the prior art and the instant claims. The selection of a known material based on its suitability for its intended use supports a case of prima facie obviousness (see MPEP 2144.07). In addition, the results shown are not commensurate in scope with the claimed range as the results detail only a single point within the claimed range. Thus one of ordinary skill in the art would not be able to ascertain a trend from the data presented to determine which concentrations of Pluronic® F68 would achieve the "unexpected" outcome (see MPEP 2145). Furthermore, the claims have not been amended to be commensurate in scope with the concentration that yielded the "unexpected" outcome, thus the criticality of the claimed range to the invention is not clear.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. Claim 6 recites the limitation "…the poloxamer" in line 1. There is insufficient antecedent basis for this limitation in the claim.

For the sake of application of prior art, this phrase is interpreted as referring to the "polyoxamers" recited in claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 6-14 are rejected under 35 U.S.C. 103(a) as being obvious over Friedl et al. (US 2005/0089575) in view of Frisbee et al (WO 99/17744).

Friedl et al. teach a pharmaceutical composition tablet comprising telmisartan and a diuretic (see title), where the telmisartan is present in a dissolving layer and the diuretic is

present in a disintegrating layer (see paragraph 15; instant claims 10 and 13). More specifically, Friedl et al. teach the composition as providing a dosage unit of 10-160 mg of telmisartan and comprising 3-50 wt% telmisartan (see paragraph 49; instant claims 1 and 11-12). This dosage unit also has a basic agent at 0.25-20 wt% such as alkali metal hydroxides like NaOH and KOH, basic amino acids, or meglumine (see paragraph 46; instant claims 1-3), where the molar ratio of telmisartan to basic agent is exemplified at nearly 2 to 1 (see example 4; instant claim 1). The dosage unit further comprises a water soluble diluent at 60-80 wt% such as carbohydrates like glucose, oligosaccharides like sucrose, and sugar alcohols like sorbitol (see paragraph 47 and 49; instant claims 1 and 7-8), Pluronic®, a trade name for a set of polyoxamers (also known as poloxamers), at 0-10 wt% (see paragraphs 55, 58, and 63; instant claim 1), and from 0-30% of other additional lubricants, binders, flow control agents, crystallization retarders, solubilizers and color agents (see paragraphs 51-58; instant claim 9). Friedl et al. does not specifically teach the Pluronic® (polyoxamer) having an average molecular weight of 2000-12000.

Frisbee et al. teach an immediate release dosage form where a variety of drugs can be utilized and within this context also teach that poloxamers (polyoxamers) are commonly known commercially available solubilizers (see abstract and page 5 lines 13-14 and 20-25). Frisbee et al. also teach that poloxamer 188, whose average molecular weight is between 7680 and 9510, is particularly effective as a solubilizer (see page 5 lines 27-28). In view of these teachings, it would have been obvious to one of ordinarily skill in the art at the time the invention was made to use poloxamer 188 as the particular solubilizer in the invention of Friedl et al.

Friedl et al. teach multiple methodologies for the production of telmisartan material used to make tablets. One embodiment in view of Frisbee et al. involves the spray drying of an aqueous solution containing telmisartan at 3-50 wt%, basic agents at 0.25-20 wt% and Pluronic® (poloxamer 188) at 1-10 wt% (see paragraphs 55, 49, 63 line 11, 84, and 85 line 1;

instant claim 14). The granulate from the spray drying process is mixed with water soluble diluent at 30-95 wt% along with a lubricant at 0.1-5 wt% (see paragraphs 91-93; instant claim 14). The resulting mixture can also contain other excipients and adjuvants (see paragraphs 51-58; instant claim 14). Therefore claims 1-3 and 6-14 are obvious over Friedl et al. in view of Frisbee et al.

Claims 1, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friedl et al. in view of Frisbee et al. as applied to claims 1-3 and 6-13 above, and further in view of Gennaro (Remington: The Science and Practice of Pharmacy Volume II), Parikh (Handbook of Pharmaceutical Granulation Technology), and the EPA Profile of the Pharmaceutical Manufacturing Industry.

Friedl et al. teach multiple methodologies for the production of telmisartan material used to make tablets. One embodiment, in view of Frisbee et al. involves the spray drying of an aqueous solution containing telmisartan at 3-50 wt%, basic agents at 0.25-20 wt% and Pluronic® (poloxamer 188) at 1-10 wt% (see paragraphs 55, 49, 63 line 11, 84, and 85 line 1; instant claim 14). The granulate from the spray drying process is mixed with water soluble diluent at 30-95 wt% along with a lubricant at 0.1-5 wt% (see paragraphs 91-93; instant claim 14). The resulting mixture can also contain other excipients and adjuvants (see paragraphs 51-58; instant claim 14). Although not specifically disclosed by Friedl et al., Parikh teaches that ethanol is also a commonly used solvent in spray drying techniques (see page 92 paragraph 1 line 3; instant claim 14); thus one of ordinary skill in the art at the time the invention was made would have found it obvious to employ ethanol as an additional solvent in the system.

Another embodiment of the invention taught by Friedl at el. in view of Frisbee et al. employs the coating of carrier particles in a fluidized bed with the aqueous solution of

telmisartan (see paragraph 38 lines 1-4). One of ordinary skill in the art at the time the invention was made would have readily recognized that fluidized bed granulation would meet this recitation (granulating solution is sprayed (coated) onto suspended (fluidized) particles which then dry rapidly in the suspending air – see Gennaro page 1625 column 2 paragraph 1 lines 1-4). As Friedl et al. clearly envisioned the combination of the water soluble diluent with the alkaline solution of telmisartan and its solubility enhancer (see paragraphs 55, 49, 63 line 11, 84, 85 line 1, and 91-93), one of ordinary skill in the art at the time the invention was made would have found it obvious to use the water soluble diluent already specified by the formulation as the "carrier particles in a fluidized bed" and the alkaline solution of telmisartan with poloxamer 188 as the granulating solution. The EPA Profile of the Pharmaceutical Manufacturing Industry teaches that ethanol is a common solvent used in the pharmaceutical industry, so it would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ ethanol as an additional solvent in the fluidized bed granulation of the composition of Friedl et al. in view of Frisbee et al. (see page 41 paragraph 2 line 13). As taught by Gennaro, the process of fluidized bed granulation involves the drying of the coated granulate (see page 1625 column 2 paragraph 1 lines 4-6). Since the particles that result from the granulation that occurs in the fluidized bed may be larger than amenable to later tablet formation (see Parikh page 244), an artisan of ordinary skill would appreciate the need to employ some methodology (e.g. milling) to reduce the particle size. The resulting mixture can also contain other excipients and adjuvants (see Friedl et al. paragraphs 51-58). Thus, claims 1-3 and 6-15 are obvious over Friedl et al. in light of Frisbee et al., Gennaro, Parikh, and the EPA Profile of the Pharmaceutical Manufacturing Industry.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 6-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of copending Application No. 11/560059 in view of Frisbee et al. Both the instant claim and those of the copending application claim a composition with telmisartan at 3-50 wt% in a dissolving matrix with a basic agent (at the same ratio relative to one another), a water-soluble diluent at 25-70 wt%, a surfactant at 1-20 wt%, and additional excipients such that all the components add to 100%. The basic agent is taught as to be chosen from the same collection of compounds, as are the water soluble diluent and additional excipients. Further the pharmaceutical dosage unit is taught to comprise the same amount of telmisartan. Both applications also teach a bi-layered tablet with telmisartan in a dissolving layer and a diuretic in a disintegrating layer. Although the copending application teaches the same class of surfactants (poloxamers), it does not teach a particular molecular weight range for them. Frisbee teaches the use of poloxamers in the weight range of 7680 to 9510, as being particularly effective as a solubilizer in a pharmaceutical

composition (see page 5 lines 27-28). Thus it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Frisbee et al. in copending Application No. 11/560059 to select a particular poloxamer as the surfactant.

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Thursday 8-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615

/Caralynne Helm/
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